

FIGURE 1

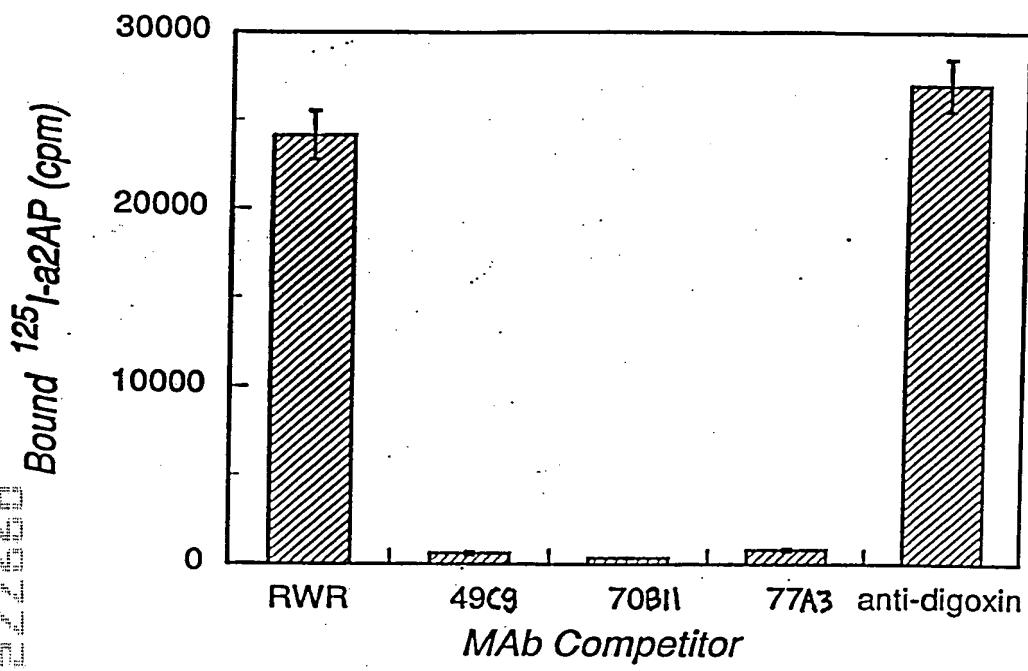


FIGURE 2

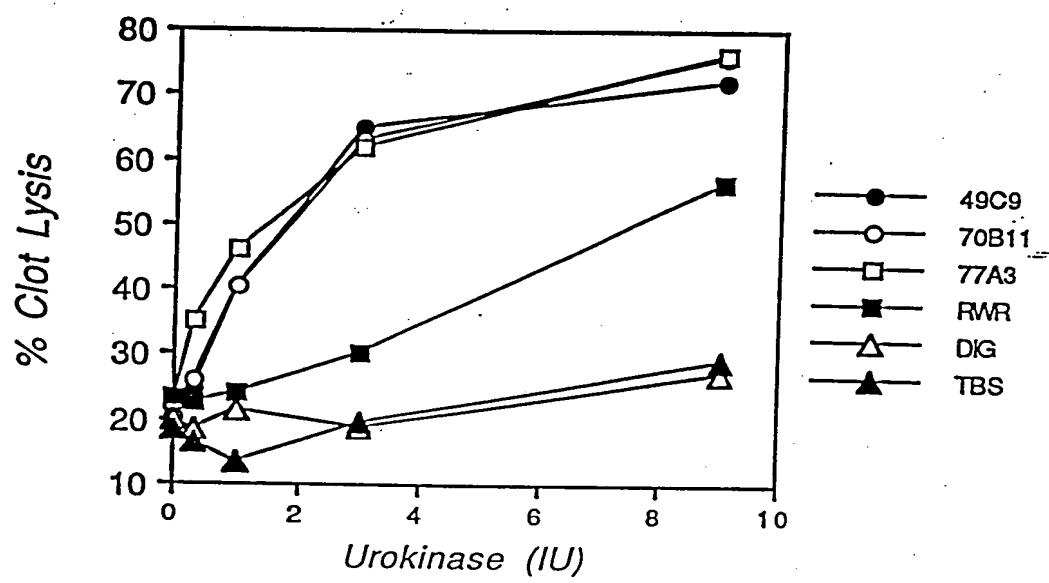


FIGURE 3

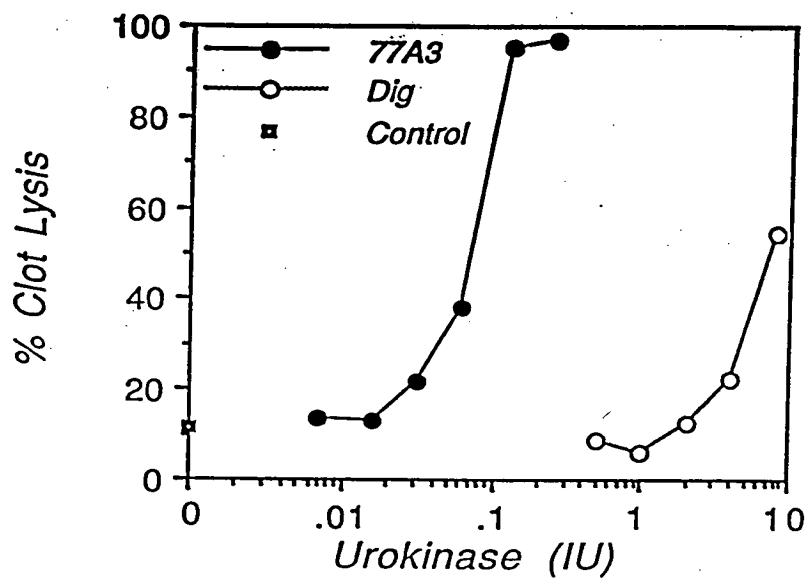
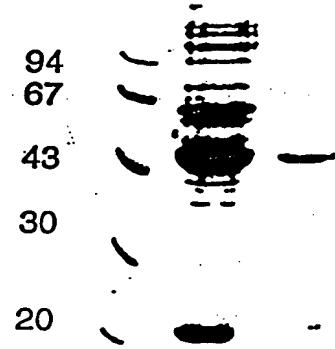


FIGURE 4



Std Ascites 77A3

FIGURE 5

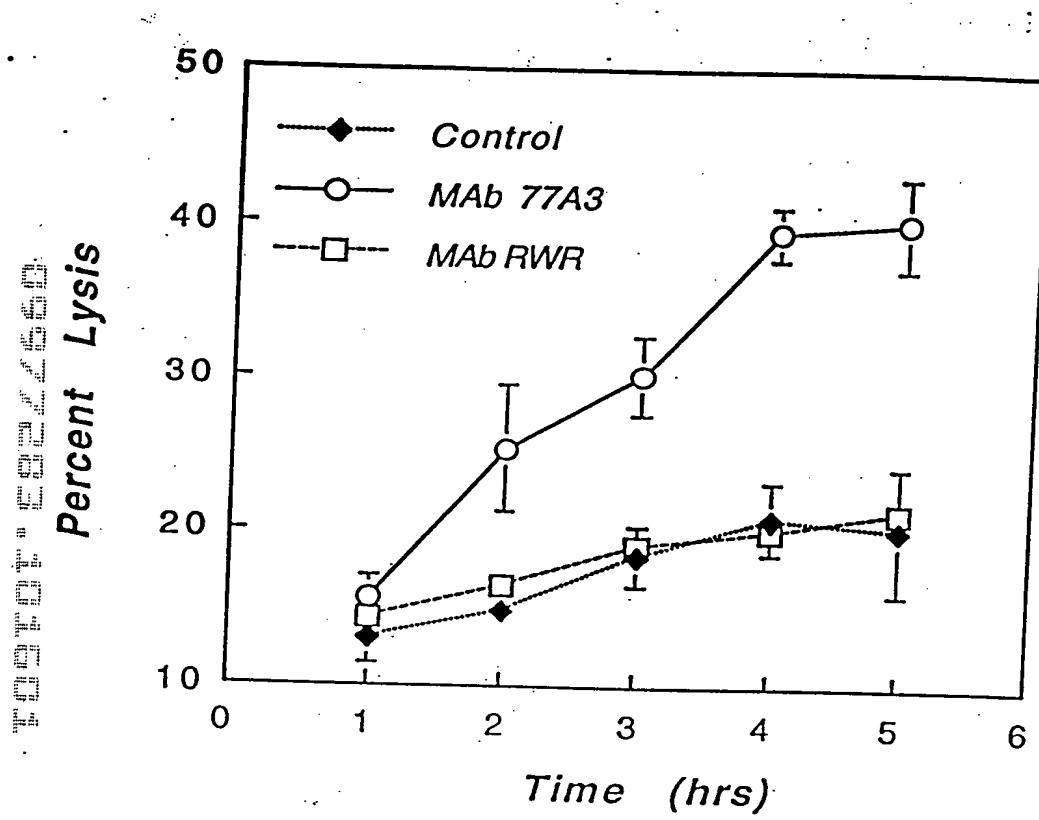


FIGURE 6

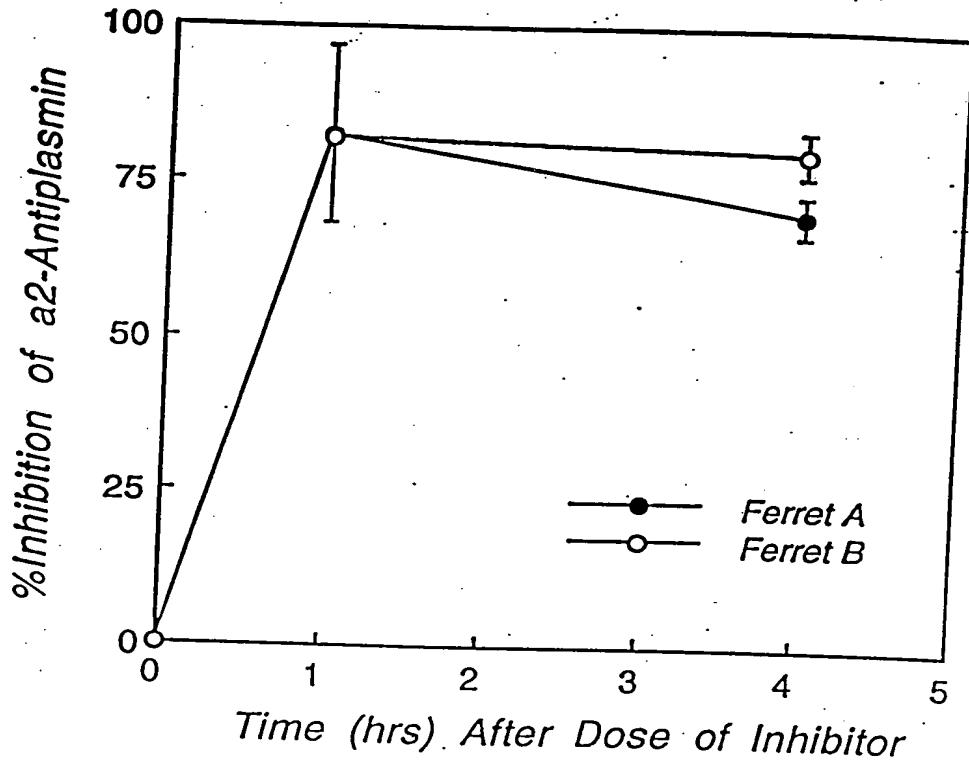


FIGURE 7

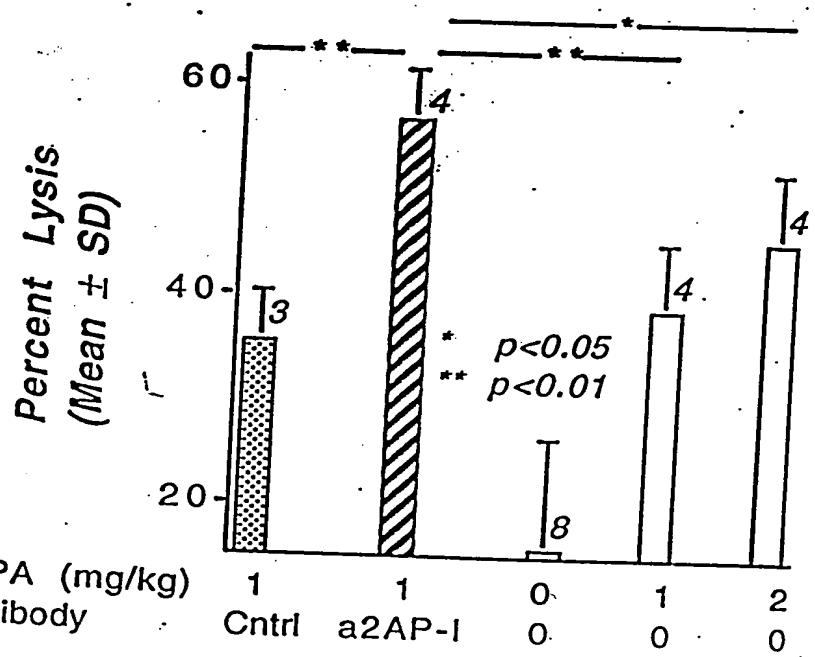


FIGURE 8

100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500

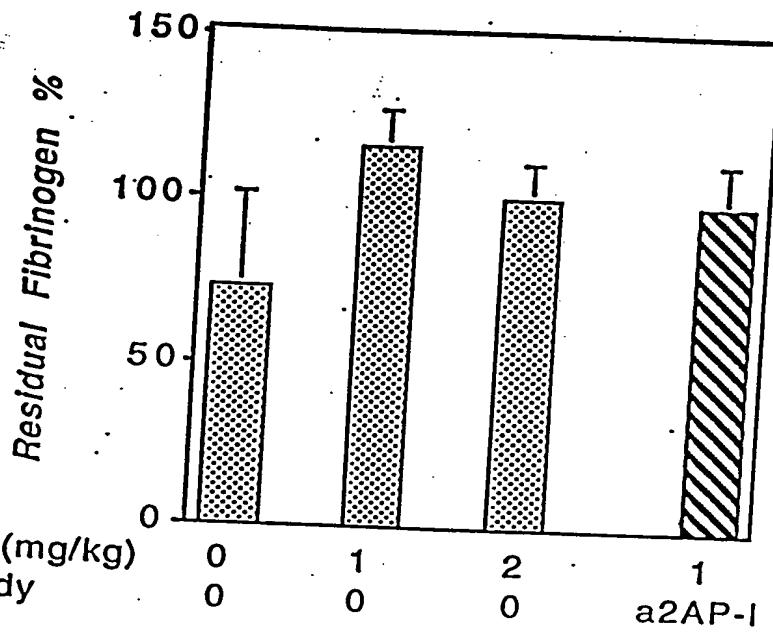


FIGURE 9

FIG. 10

MAb Light Chain Amino Terminal Sequence

49C9 xIQMTQSPASLSASV

70B11 DIQMT

77A3 xIQMTQSPASLSASV

Fig. 11

10	20	30	40	50	60
*	*	G *	*	*	*
ATGAGTGTGC TCACTCAGGT CCTGGCGTTG CTGCTGCTGT GGCTTACAGG TGCCAGATGT					
M	S	V	L	T	Q V L G L L L L W L T G A R C>
					A
70	80	90	100	110	120
*	*	*	*	*	*
GACATCCAGA TGACTCAGTC TCCAGCCTCC CTATCTGCAT CTGTGGGAGA AACTGTCACC					
D	I	Q	M	T	Q S P A S L S A S V G E T V T>
130	140	150	160	170	180
*	*	*	*	*	*
ATCACATGTC GAGCAAGTGG GAATATTCAC AATTATTTAG CATGGTATCA GCAGAAACAG					
I	T	C	R	A	S G N I H N Y L A W Y Q Q K Q>
190	200	210	220	230	240
*	*	*	*	*	*
GGAAAATCTC CTCAGCTCCT GGTCTATAAT GCAAAAACCT TAGCAGATGG TGTGCCATCA					
G	K	S	P	Q	L L V Y N A K T L A D G V P S>
250	260	270	280	290	300
*	*	*	*	*	*
AGGTTCACTG GCAGTGGATC AGGAACACAA TTTTCTCTCA GGATCAACAG CCTGCAGCCT					
R	F	S	G	S	G T Q F S L R I N S L Q P>
310	320	330	340	350	360
*	*	*	*	*	*
GAAGATTTG GGAGTCATTA CTGTCAACAT TTTTGGACCA CTCCGTGGAC GTTCGGTGGAA					
E	D	F	G	S	H Y C Q H F W T T P W T F G G>
370	380				
*	*				
GGCACCAAGC TGGAAATCAA A					
G	T	K	L	E	I K

Fig. 12

FIG. 13

10	20	30	40	50	60
*	*	*	*	*	*
ATGAGTGTGC TCACTCAGGT CCTGGCGTTG CTGCTGCTGT GGCTTACAGG TGCCAGATGT					
M	S	V	L	T	Q
V	L	A	L	L	L
W	L	T	G	A	R
C>					
70	80	90	100	110	120
*	*	*	*	*	*
GACATCCAGA TGACTCAGTC TCCAGCCTCC CTATCTGCAT CTGTGGGAGA AACTGTCACC					
D	I	Q	M	T	Q
I	S	P	A	S	L
S	A	A	S	V	G
A	S	V	G	E	T
C>	V	T	V	T>	
130	140	150	160	170	180
*	*	*	*	*	*
ATCACATGTC GAGCAAGTGG GAATATTACAC AATTATTAG CATGGTATCA GCAGAACAG					
I	T	C	R	A	S
T	C	R	A	S	G
N	I	H	N	Y	L
A	W	Y	Q	Q	K
Q>	Q	K	Q	Q	Q>
190	200	210	220	230	240
*	*	*	*	*	*
GGAAAATCTC CTCAACTCCT GGTCTATAAT GCAAAAACCT TAGCAGATGG TGTGCCATCA					
G	K	S	P	Q	L
K	S	P	Q	L	L
V	Y	N	A	K	T
A	W	Y	L	A	D
V	P	S	G	V	P
S>	S>	S>	S>	S>	S>
250	260	270	280	290	300
*	*	*	*	*	*
AGGTTCACTG GCAGTGGATC AGGAACACAA TTTTCTCTCA AGATCAACAG CCTGCAGCCT					
R	F	S	G	S	G
F	S	G	S	G	T
T	Q	F	S	L	K
Q	P	W	A	I	N
P>	P>	P>	P>	P>	P>
310	320	330	340	350	360
*	*	*	*	*	*
GAAGATTTG GGAGTCATTA CTGTCAACAT TTTTGGACCA CTCCGTGGAC GTTCGGTGGAA					
E	D	F	G	S	H
D	F	G	S	H	Y
F	G	H	C	Q	H
G	H	H	F	W	T
H	T	T	W	P	T
T>	T>	T>	T>	T>	T>
370	380				
*	*				
GGCACCAAGC TGGAAATCAA A					
G	T	K	L	E	I
T	K	L	E	I	K

H2 HC (49c9 heavy chain) Fig. 14

9	19	29	39	49	59
*	*	*	*	*	*
ATGGMTTGG	GTGTGGAMCT	TGCTATTCCCT	GATGGCAGCT	GCCCAAAGTC	TCCAAGCACA
M A W	V W N	L L F	L M A A	A Q S	L Q A Q >
D	T				
69	79	89	99	109	119
*	*	*	*	*	*
GATCCAGTTG	GTGCAGTCTG	GACCTGAGCT	GAAGAAGCCT	GGAGAAACAG	TCAAGATCTC
I Q L	V Q S	G P E	L K K P	G E T	V K I S >
129	139	149	159	169	179
*	*	*	*	*	*
CTGCAAGGCC	TCTGGGTATA	CCTTCACAAA	CTATGGAATG	AACTGGGTGA	AGCAGGCTCC
C K A	S G Y	T F T	N Y G M	N W V	K Q A P >
189	199	209	219	229	239
*	*	*	*	*	*
AGGAAAGGGT	TTAAAGTGGA	TGGGCTGGAT	AAACACCAAG	AGTGGAGAGC	CAACATATGC
G K G	L K W	M G W	I N T	K S G E	P T Y A >
249	259	269	279	289	299
*	*	*	*	*	*
TGAAGAGTTC	AAGGGACGGT	TTGTCTTCTC	TTTGGAAACC	TCTGCCAGCA	CTGCCCATTT
E E F	K G R	F V F S	L E T	S A S	T A H L >
309	319	329	339	349	359
*	*	*	*	*	*
GCAGATCAAG	AATTCAGAA	ATGAGGGACAC	GGCTACATAT	TTCTGTGCAA	GATGGGTACC
Q I K	N F R	N E D T	A T Y	F C A	R W V P >
369	379	389	399	409	
*	*	*	*	*	
TGGGACCTAT	GCTATGGACT	ACTGGGGTCA	AGGAACCTCA	GTCACCGTCT	CCTCA
G T Y	A M D	Y W G Q	G T S	V T V	S S >

H3 HC (70B11 heavy chain) Fig. 15

10	20	30	40	50	60
*	*	*	*	*	*
ATGGMTTGGG	TGTGGAMCTT	GCTATTCTG	ATGGCAGCTG	CCCAAAGTAT	CCAAGCACAG
M A W	V W N L	L F L	M A A	A Q S I	Q A Q >
D	T				
70	80	90	100	110	120
*	*	*	*	*	*
ATCCAGTTGG	TGCAGTCTGG	ACCTGAGCTG	AAGAAGCCTG	GAGAGACAGT	CAAGATCTCC
I Q L	V Q S G	P E L	K K P	G E T V	K I S >
130	140	150	160	170	180
*	*	*	*	*	*
TGCAAGGCTT	CTGGGTATAC	CTTCACAAAG	TATGGAATGA	ACTGGGTGAA	GCAGGCTCCA
C K A	S G Y T	F T K	Y G M	N W V K	Q A P >
190	200	210	220	230	240
*	*	*	*	*	*
GGAAAGGGTT	TAAAGTGGAT	GGGCTGGATA	AACACCAACA	GTGGAGAGCC	AACATATGCT
G K G	L K W M	G W I	N T N	S G E P	T Y A >
250	260	270	280	290	300
*	*	*	*	*	*
GAAGAGTTCA	AGGGACGGTT	TGCCTTCTCT	TTGGAAACCT	CTGCCAGCAC	TGCCTATTTG
E E F	K G R F	A F S	L E T	S A S T	A Y L >
310	320	330	340	350	360
*	*	*	*	*	*
CAGATCAACA	ACCTCAAAAA	TGAGGACTCG	GCTACATATT	TCTGTGCAAG	ATGGGTACCT
Q I N	N L K N	E D S	A T Y	F C A R	W V P >
370	380	390	400	410	
*	*	*	*	*	
GGGACCTATG	CTATGGACTA	CTGGGGTCAA	GGAACCTCAG	TCACCGTCTC	CTCA
G T Y	A M D Y	W G Q	G T S	V T V S	S >

H4 HC (77A3 heavy chain) Fig. 16

10	20	30	40	50	60
*	*	*	*	*	*
ATGGMTTGGG	TGTGGAMCTT	GCTATTCTG	ATGGCAGCTG	CCCAAAGTAT	CCAAGCACAG
M A W	V W N L	L F L	M A A	A Q S I	Q A Q >
D	T				
70	80	90	100	110	120
*	*	*	*	*	*
ATCCAGTTGG	TGCAGTCTGG	ACCTGAGCTG	AAGAACGCTG	GAGAACAGT	CAAGATCTCC
I Q L	V Q S G	P E L	K K P	G E T V	K I S >
130	140	150	160	170	180
*	*	*	*	*	*
TGCAAGGCTT	CTGGGTATAAC	CTTCACAAAC	TATGGAATGA	ACTGGGTGAA	GCAGGCTCCA
C K A	S G Y T	F T N	Y G M	N W V K	Q A P >
190	200	210	220	230	240
*	*	*	*	*	*
GGAAAGGGTT	TAAAGTGGAT	GGGCTGGATA	AACACCAAGA	GTGGAGAGCC	AACATATGCT
G K G	L K W M	G W I	N T K	S G E P	T Y A >
250	260	270	280	290	300
*	*	*	*	*	*
GAAGAGTTCA	AGGGACGGTT	TGCCTTCTCT	TTGGAAACCT	CTGCCAGCAC	TGCCAATTTG
E E F	K G R F	A F S	L E T	S A S T	A N L >
310	320	330	340	350	360
*	*	*	*	*	*
CAGATCAAGA	ACCTCAAAAA	TGAGGGACACG	GCTACATATT	TCTGTGCAAG	ATGGGTACCT
Q I K	N L K N	E D T	A T Y	F C A R	W V P >
370	380	390	400	410	
*	*	*	*	*	
GGGACCTATG	CCATGGACTA	CTGGGGTCAA	GGAACCTCAG	TCACCGTCTC	CTCA
G T Y	A M D Y	W G Q	G T S	V T V S	S S

h7A3-1 and h7A3-2 LIGHT CHAIN

Signal Peptide

ATT TAA ATT GAT ATC TCC TTA CGT CTC GAG

Humanized fit (sense)

Humanized in (anti-sense)

h 77A3V L

Humanized (aa)

ମୁଦ୍ରଣ

Organized in (anti-sense)

Figure 17

• L1 Loop

2	7	2	3	3	1	a	b	c	d	e	1	2	3	4
6														
T	I	T	C	R	A	S	G	N	I	H	N			
ACE	ATC	ACA	ATC											
TGT	TAC													

Humanized (aa)
Humanized n (sense)
Humanized n (anti-sense)

Humanized (ea) \backslash 77A
 Humanized in (sense)
 Humanized in (anti-sense)

1000
3

9	9	a	b	c	d	e	9
0	0	H	F	W	T	P	0
1	1	Q	Q	Q	Q	Q	1
2	2	Q	Q	Q	Q	Q	2
3	3	Q	Q	Q	Q	Q	3
4	4	Q	Q	Q	Q	Q	4
5	5	Q	Q	Q	Q	Q	5
6	6	Q	Q	Q	Q	Q	6
7	7	Q	Q	Q	Q	Q	7
8	8	Q	Q	Q	Q	Q	8
9	9	Q	Q	Q	Q	Q	9
10	10	Q	Q	Q	Q	Q	10
11	11	Q	Q	Q	Q	Q	11
12	12	Q	Q	Q	Q	Q	12
13	13	Q	Q	Q	Q	Q	13
14	14	Q	Q	Q	Q	Q	14
15	15	Q	Q	Q	Q	Q	15
16	16	Q	Q	Q	Q	Q	16
17	17	Q	Q	Q	Q	Q	17
18	18	Q	Q	Q	Q	Q	18
19	19	Q	Q	Q	Q	Q	19
20	20	Q	Q	Q	Q	Q	20
21	21	Q	Q	Q	Q	Q	21
22	22	Q	Q	Q	Q	Q	22
23	23	Q	Q	Q	Q	Q	23
24	24	Q	Q	Q	Q	Q	24
25	25	Q	Q	Q	Q	Q	25
26	26	Q	Q	Q	Q	Q	26
27	27	Q	Q	Q	Q	Q	27
28	28	Q	Q	Q	Q	Q	28
29	29	Q	Q	Q	Q	Q	29
30	30	Q	Q	Q	Q	Q	30
31	31	Q	Q	Q	Q	Q	31
32	32	Q	Q	Q	Q	Q	32
33	33	Q	Q	Q	Q	Q	33
34	34	Q	Q	Q	Q	Q	34
35	35	Q	Q	Q	Q	Q	35
36	36	Q	Q	Q	Q	Q	36
37	37	Q	Q	Q	Q	Q	37
38	38	Q	Q	Q	Q	Q	38
39	39	Q	Q	Q	Q	Q	39
40	40	Q	Q	Q	Q	Q	40
41	41	Q	Q	Q	Q	Q	41
42	42	Q	Q	Q	Q	Q	42
43	43	Q	Q	Q	Q	Q	43
44	44	Q	Q	Q	Q	Q	44
45	45	Q	Q	Q	Q	Q	45
46	46	Q	Q	Q	Q	Q	46
47	47	Q	Q	Q	Q	Q	47
48	48	Q	Q	Q	Q	Q	48
49	49	Q	Q	Q	Q	Q	49
50	50	Q	Q	Q	Q	Q	50
51	51	Q	Q	Q	Q	Q	51
52	52	Q	Q	Q	Q	Q	52
53	53	Q	Q	Q	Q	Q	53
54	54	Q	Q	Q	Q	Q	54
55	55	Q	Q	Q	Q	Q	55
56	56	Q	Q	Q	Q	Q	56
57	57	Q	Q	Q	Q	Q	57
58	58	Q	Q	Q	Q	Q	58
59	59	Q	Q	Q	Q	Q	59
60	60	Q	Q	Q	Q	Q	60
61	61	Q	Q	Q	Q	Q	61
62	62	Q	Q	Q	Q	Q	62
63	63	Q	Q	Q	Q	Q	63
64	64	Q	Q	Q	Q	Q	64
65	65	Q	Q	Q	Q	Q	65
66	66	Q	Q	Q	Q	Q	66
67	67	Q	Q	Q	Q	Q	67
68	68	Q	Q	Q	Q	Q	68
69	69	Q	Q	Q	Q	Q	69
70	70	Q	Q	Q	Q	Q	70
71	71	Q	Q	Q	Q	Q	71
72	72	Q	Q	Q	Q	Q	72
73	73	Q	Q	Q	Q	Q	73
74	74	Q	Q	Q	Q	Q	74
75	75	Q	Q	Q	Q	Q	75
76	76	Q	Q	Q	Q	Q	76
77	77	Q	Q	Q	Q	Q	77
78	78	Q	Q	Q	Q	Q	78
79	79	Q	Q	Q	Q	Q	79
80	80	Q	Q	Q	Q	Q	80
81	81	Q	Q	Q	Q	Q	81
82	82	Q	Q	Q	Q	Q	82
83	83	Q	Q	Q	Q	Q	83
84	84	Q	Q	Q	Q	Q	84
85	85	Q	Q	Q	Q	Q	85
86	86	Q	Q	Q	Q	Q	86
87	87	Q	Q	Q	Q	Q	87
88	88	Q	Q	Q	Q	Q	88
89	89	Q	Q	Q	Q	Q	89
90	90	Q	Q	Q	Q	Q	90
91	91	Q	Q	Q	Q	Q	91
92	92	Q	Q	Q	Q	Q	92
93	93	Q	Q	Q	Q	Q	93
94	94	Q	Q	Q	Q	Q	94
95	95	Q	Q	Q	Q	Q	95
96	96	Q	Q	Q	Q	Q	96
97	97	Q	Q	Q	Q	Q	97
98	98	Q	Q	Q	Q	Q	98
99	99	Q	Q	Q	Q	Q	99
100	100	Q	Q	Q	Q	Q	100

Humanized (aa)
Humanized in (sense)
Humanized in (anti-sense)

7.1.3-1 HEAVY CHAIN SEQUENCES

Figure 18

Signal Peptide

67743-1

Humanized (as)
Humanized in (sense)
Humanized in (anti-sense)

Humanized (as)
Humanized in (sense)
Humanized in (anti-sense)

Humanized (aa)
Humanized nt (sense)
Humanized nt (sense)

77A3-1

Humanized (aa)
Humanized ni (sense)

TA YI SSI

S E L K P G A S V K I S C K A S G

E F K G R

卷之六

SEIKI
SACCTGAGCTGAG
—
TTAGA CTC GAG TTC ATT

K
N T
ACC
TCC

G GAC ACG CCT GTC TAT
C CTC TCC CCA CAC ATTC

Q 1 V Q S C

G 2 1

2181

h 77A3.1

h77A3-2 HEAVY CHAIN SEQUENCES

Figure 19

Humanized (aa)
Humanized in (sense)
Humanized in (anti-sense)

Signal Peptide

Humanized in (anti-sense)
Humanized in (sense)
Humanized in (anti-sense)

Figure 20

Plasmin Assay
Murine, Chimeric and Humanized 77A3
6/3/97

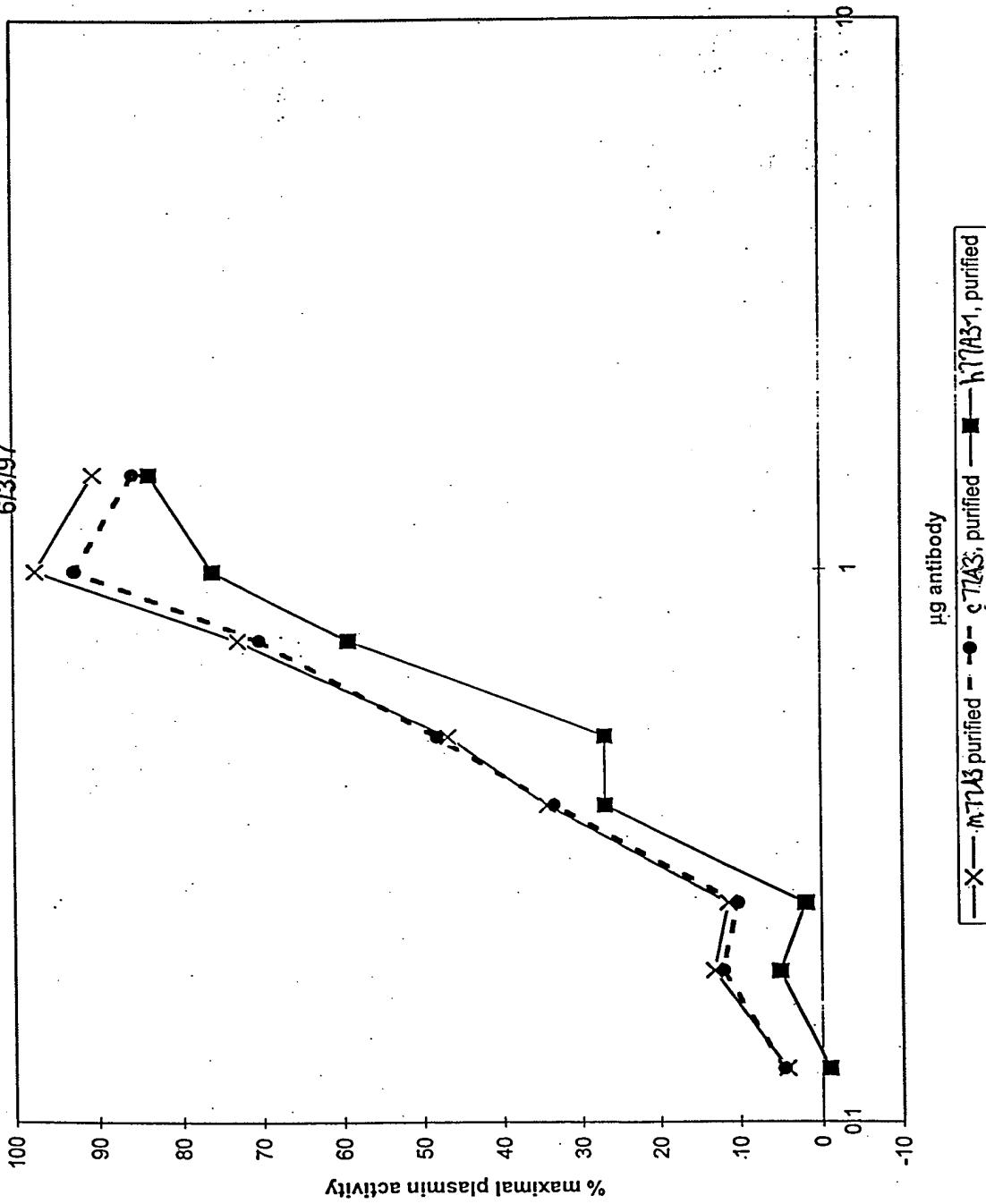


Figure 21

α 2-antiplasmin antibody light chain sequences

h77A3-1 and h77A3-2

D I Q M T Q S P S S L S A S V G D R V T I T C R A S G N I H N	Y L A
D I Q M T Q S P A S L S A S V G E T V T I T C R A S G N I H N	Y L A
D I Q M T Q S P A S L S A S V G E T V T I T C R A S G N I H N	Y L A
D I Q M T Q S P A S L S A S V G E T V T V T C R A S G N I H N	Y L A
D I Q M T Q S P A S L S A S V G E T V T X T C R A S G N I H N	Y L A
D I Q M T Q S P A S L S A S V G E T V T I T C R A S G N I H N	Y L A
D I Q M T Q S P X S L S A S V G X X V T X T C R A S G N I H N	Y L A

murine consensus
77A3/49C9 consensus
all

12 Loop

	5		6		7	
WYQQKQGKSPQLLVYNAK	TLAS	GVPSRFSGSGSGTDFTLT				
WYQQKQGKSPQLLVYNAK	TLAD	GVPSRFSGSGSGTQFSLK				
WYQQKQGKSPQLLVYNAK	TLAD	GVPSRFSGSGSGTQFSLR				
WYQQKQGKSPQLLVYNAK	TLAD	GVPSRFSGSGSGTQYSLK				
WYQQKQGKSPQLLVYNAK	TLAD	GVPSRFSGSGSGTQXSLX				
WYQQKQGKSPQLLVYNAK	TLAD	GVPSRFSGSGSGTQFSLX				
WYQQKQGKSPQLLVYNAK	TLAX	GVPSRFSGSGSGTXXXLX				

murine consensus 77A3/49C9 consensus align

L3 Loop																																
7	8	9	p	s	a	b	c	d	e	f	g	10	11	12																		
I	S	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	G	G	T	K	L	E	I	H
I	N	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	Q	G	T	K	L	E	I	H
I	N	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	Q	Q	T	K	L	E	I	H
I	N	S	L	Q	P	E	D	F	G	S	Y	Y	C	Q	H	F	W	S	N	P	W	T	F	G	G	G	T	K	L	E	I	H
I	N	S	L	Q	P	E	D	F	G	S	X	Y	C	Q	H	F	W	X	X	P	W	T	F	G	G	G	T	K	L	E	I	H
I	N	S	L	Q	P	E	D	F	G	S	H	Y	C	Q	H	F	W	T	T	P	W	T	F	G	Q	G	T	K	L	E	I	H
I	X	S	L	Q	P	E	D	F	G	S	X	Y	C	Q	H	F	W	X	X	P	W	T	F	G	G	G	T	K	L	E	I	H

Figure 22

α 2-antiplasmin antibody heavy chain sequences

	H1 Loop																
h77A3-1	Q	I	Q	L	V	Q	S	G	S	E							
h77A3-2	I	Q	L	V	Q	S	G	A	E	V							
m77A3	Q	I	Q	L	V	Q	S	G	S	P							
m49C9	I	Q	L	V	Q	S	G	P	E	L							
m70B11	I	Q	L	V	Q	S	G	P	E	L							
humanized consensus	Q	I	Q	L	V	Q	S	G	S	X							
murine consensus	I	Q	L	V	Q	S	G	S	X	K							
77A3/49C9 consensus	I	Q	L	V	Q	S	G	S	X	K							
all	I	Q	L	V	Q	S	G	S	X	X							
	Q	I	Q	L	V	Q	S	G	S	X							
	I	Q	L	V	Q	S	G	S	X	K							
	I	Q	L	V	Q	S	G	S	X	X							
	I	Q	L	V	Q	S	G	S	X	X							
	H2 Loop																
h77A3-1	G	L	E	W	M	G	W	I	N	T							
h77A3-2	G	L	E	W	M	G	W	I	N	T							
m77A3	G	L	K	W	M	G	W	I	N	T							
m49C9	G	L	K	W	M	G	W	I	N	T							
m70B11	G	L	K	W	M	G	W	I	N	T							
humanized consensus	G	L	E	W	M	G	W	I	N	T							
murine consensus	G	L	K	W	M	G	W	I	N	T							
77A3/49C9 consensus	G	L	E	W	M	G	W	I	N	T							
all	G	L	E	W	M	G	W	I	N	T							
	G	L	E	W	M	G	W	I	N	T							
	G	L	K	W	M	G	W	I	N	T							
	G	L	K	W	M	G	W	I	N	T							
	G	L	X	W	M	G	W	I	N	T							
	H3 Loop																
h77A3-1	K	A	E	D	T	A	V	Y	F	C	A	R	W	V	P	G	T
h77A3-2	R	S	D	D	T	A	V	Y	F	C	A	R	W	V	P	G	T
m77A3	K	N	E	D	T	A	V	Y	F	C	A	R	W	V	P	G	T
m49C9	R	N	E	D	T	A	V	Y	F	C	A	R	W	V	P	G	T
m70B11	K	N	E	D	S	A	T	Y	F	C	A	R	W	V	P	G	T
humanized consensus	X	X	D	T	A	V	Y	F	C	A	R	W	V	P	G	T	
murine consensus	X	N	E	D	X	A	T	Y	F	C	A	R	W	V	P	G	T
77A3/49C9 consensus	X	N	E	D	T	A	V	Y	F	C	A	R	W	V	P	G	T
all	X	X	D	X	A	X	Y	F	C	A	R	W	V	P	G	T	
	X	X	D	T	A	V	Y	F	C	A	R	W	V	P	G	T	
	X	N	E	D	T	A	V	Y	F	C	A	R	W	V	P	G	T
	X	N	E	D	S	A	T	Y	F	C	A	R	W	V	P	G	T
	X	X	D	X	A	X	Y	F	C	A	R	W	V	P	G	T	